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| 10/799,514 | 03/12/2004 | Francois Spertini | 30985/41486 | 8487 |

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| EXAMINER | |
|---|---|
| ROONEY, NORA MAUREEN | |

| ART UNIT | PAPER NUMBER |
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| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/799,514 | SPERTINI ET AL. | |
| | Examiner | Art Unit | |
| | NORA M. ROONEY | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *55-63 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-63 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. Applicant's response filed on 12/01/2009 and sequence listing filed on 05/26/2010 is acknowledged.

2. Claims 55-63 and 65 are pending and currently under examination as they read on a method for generating a composition of contiguous overlapping peptide fragments.

3. The following rejections are necessitated by the amendment filed on 12/01/2009.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 55-61 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 (PTO-892 mailed on 06/12/2008; Reference N) in view of each of Von Garnier er al. (Reference C24; 07/26/2004); Astori et al. (Reference C16; IDS filed on 07/26/2004); Fellrath et al. (Reference C17; IDS filed on 07/26/2004); Kammerer et al.(Reference C8; IDS filed on 06/22/2004); and Kammerer et al.(Reference C9; IDS filed on 06/22/2004).

WO 01/88085 teaches a method for generating a composition of contiguous overlapping peptide fragments (COPs) for a selected polypeptide allergen the improvement comprising

carrying out the steps of: (1) determining candidate contiguous overlapping peptides by a method comprising: (a) conducting a computerized structural analysis of the selected polypeptide allergen to identify alpha helix, beta sheet and cysteine bridge three-dimensional structural formations (In particular, page 8, lines 5-15); (b) selecting one or more separation sites within the sequence of the polypeptide allergen to provide candidate contiguous overlapping peptide fragments from 30 to 90 peptides in length which peptides overlap each separation site (In particular, page 2, lines 16-23) wherein said COPs present all potential T-cell epitopes but interrupt alpha helix and beta-sheet structural motifs involved in IgE binding (In particular, page 19, lines 13-29); and (2) producing said candidate contiguous overlapping peptide fragments; and (3) screening said candidate COPs by the steps of: (a) selecting COPs characterized by having a T cell stimulating activity for T cells specific for the selected polypeptide allergen which is greater than a selected minimum by contacting said COPs with T cells specific for the selected polypeptide allergen and detecting said T cell stimulating activity (In particular, page 9, line 31 to page 10, line 9); and (b) selecting COPs characterized by having an IgE binding activity for IgEs reactive with the selected polypeptide allergen which is less than a selected maximum by contacting said COPs with IgEs reactive with said selected polypeptide allergen and detecting said IgE binding activity by in vitro and in vivo tests (In particular, page 6, line 5 to page 7, line 12) of claim 55; wherein the COPs have relatively reduced levels of IgE binding activity but conserved T cell stimulating activities relative to the IgE binding and T cell stimulating activities of the allergen (In particular, page 19, lines 13-29);) of claim 56; wherein the peptides overlap each separation site by 10 amino acid residues (In particular, page 2, lines 16-23) of claim 57; wherein said COPs have a T cell stimulating index which is greater than 2

(In particular, page 9, line 31 to page 10, line 9) of claim 58; wherein said COPs are useful in inducing tolerance to said polypeptide allergen (In particular, page 6, lines 27-30) of claim 59; wherein the COPs are useful in desensitization immunotherapy (In particular, page 18, lines 9-30) of claim 60; and wherein which the IgE binding activity in vitro is measured by immunoblotting (In particular page 24, lines 15-29) of claim 61; and wherein the IgE binding activity is measured in vivo by an intradermal test (In particular, page 6, lines 27-30, page 3, lines 8-13) of claim 63.

The claimed invention differs from the prior art in the recitation of "sets of COPs" in claims 55-56, 58-60 and 65.

Von Garnier er al. teaches a composition comprising a set of three overlapping 44-60-mer peptides spanning the entirety of the phospholipase a2 allergen. The fragments overlap each other by at least 10 amino acids and the composition is used for allergen immunotherapy (In particular, Figure 1, page 1643, whole document).

Astori et al. teaches a composition comprising a set of three overlapping 44-60-mer peptides spanning the entirety of the phospholipase a2 allergen. The fragments overlap each other by at least 10 amino acids and the composition is used for allergen immunotherapy (In particular, whole document, materials and methods section, Figure 1).

Fellrath et al. teaches a composition comprising a set of three overlapping 44-60-mer peptides spanning the entirety of the phospholipase a2 allergen. The fragments overlap each other by at least 10 amino acids and the composition is used for allergen immunotherapy (In particular, whole document, methods section).

Kammerer et al. teaches a composition comprising a set of three overlapping 40-60-mer peptides spanning the entirety of the phospholipase a2 allergen. The fragments overlap each other by at least 10 amino acids and the composition is used for allergen immunotherapy (In particular, page 99, right column, whole document).

Kammerer et al. teaches a composition comprising a set of three overlapping 40-60-mer peptides spanning the entirety of the phospholipase a2 allergen. The fragments overlap each other by at least 10 amino acids and the composition is used for allergen immunotherapy (In particular, page 1017, left column, whole document).

It would have been obvious to apply the teachings of allergen peptide sets taught in Von Garnier er al. (Reference C24; 07/26/2004); Astori et al. (Reference C16; IDS filed on 07/26/2004); Fellrath et al. (Reference C17; IDS filed on 07/26/2004); Kammerer et al.(Reference C8; IDS filed on 06/22/2004); and Kammerer et al.(Reference C9; IDS filed on 06/22/2004) to the teaching of WO 01/88085 teaches a method for generating a composition of contiguous overlapping peptide fragments. The Von Garnier er al. (Reference C24; 07/26/2004); Astori et al. (Reference C16; IDS filed on 07/26/2004); Fellrath et al. (Reference C17; IDS filed

on 07/26/2004); Kammerer et al.(Reference C8; IDS filed on 06/22/2004); and Kammerer et al.(Reference C9; IDS filed on 06/22/2004) references each teach that the sets are useful for immunotherapy since they have retained all of the allergen T cell epitopes, but lack IgE binding epitopes.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

6. Claims 55 and 61- 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 (PTO-892; Reference N) in view of each of Von Garnier er al. (Reference C24; 07/26/2004); Astori et al. (Reference C16; IDS filed on 07/26/2004); Fellrath et al. (Reference C17; IDS filed on 07/26/2004); Kammerer et al.(Reference C8; IDS filed on 06/22/2004); and Kammerer et al.(Reference C9; IDS filed on 06/22/2004) and further in view of Shanti et al. (PTO-892 mailed 02/12/2007, Page 2, Reference U) .

WO 01/88085; Von Garnier er al. ; Astori et al.; Fellrath et al.; Kammerer et al.; and Kammerer et al. have been discussed *supra*.

The claimed invention differs from the prior art by the recitation of "wherein the immunoblot is a dot blot" of claim 62.

Shanti et al. uses a dot-blot technique to determine IgE binding to Sa-II and tropomyosin shrimp allergen peptide fragments (In particular, page 5356, paragraph spanning left and right columns and Figure 1).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Shanti et al. to the teachings of WO 01/88085 and each of Von Garnier er al. ; Astori et al.; Fellrath et al.; Kammerer et al.; and Kammerer et al. to determine IgE binding activity to overlapping peptide fragment sets using a dot blot assy.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because the dot blot as taught by Shanti et al. is a good way to test for IgE binding activity to allergen fragments (In particular, page 5356, paragraph spanning left and right columns, abstract, Figure 1). The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

7. Claims 55, 63 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/88085 (PTO-892; Reference N) in view of each of Von Garnier er al. (Reference C24; 07/26/2004); Astori et al. (Reference C16; IDS filed on 07/26/2004); Fellrath et al. (Reference C17; IDS filed on 07/26/2004); Kammerer et al.(Reference C8; IDS filed on 06/22/2004); and Kammerer et al.(Reference C9; IDS filed on 06/22/2004) and further in view of Spertini et al. (IDS filed on 07/26/2004).

WO 01/88085; Von Garnier er al. ; Astori et al.; Fellrath et al.; Kammerer et al.; and Kammerer et al. have been discussed *supra*.

The claimed invention differs from the prior art by the recitation of "wherein the intradermal test is an immediate intradermal (ID) test wherein the sets of COPs are selected which have a wheal diameter less than or equal to 5 mm at a peptide concentration of greater than 0.1 pg/ml and no flare reaction" of claim 65.

Spertini et al. teaches the intradermal injection of three long (44-60 amino acid long) overlapping peptides at a peptide concentration of .1 μg/ml in 9 patients. Only 3 of the patients exhibited a positive reaction at day 70. The reference is silent as to what is defined as a positive reaction, but 6 of the 9 patients exhibited no reaction. Therefore, 6 of the patients had no reaction, so they exhibited no flare reaction and a wheal diameter of less than 5mm in response to the 1 pg/ml intradermal injection.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Spertini et al. to those of WO 01/88085 and each of WO 01/88085; Von Garnier er al. ; Astori et al.; Fellrath et al.; Kammerer et al.; and Kammerer et al in order to measure the IgE binding activity of the sets of long overlapping peptides in vivo at a relevant concentration because in vivo data more reliably confirms the applicability of the long overlapping peptide sets for an effective immunotherapy technique. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5- 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A

message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 16, 2010

/Nora M Rooney/

Primary Examiner, Art Unit 1644